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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,950	08/11/2005	Christopher J. Speirs	SPEI3002	1941

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EXAMINER	
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ART UNIT	PAPER NUMBER
1615	

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10/05/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,950	SPEIRS ET AL.	
	Examiner	Art Unit	
	S. TRAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63-92* is/are pending in the application.

4a) Of the above claim(s) *66-68,72-75 and 92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63-65,69-71 and 76-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of species 1 a, 2 a, and 3 a in the reply filed on 07/20/10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 66-68, 72-75 and 92 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07/20/20.

Claim Rejections - 35 USC § 102

Claims 63-65, 69-71 and 79 are rejected under 35 U.S.C. 102(e) as being anticipated by Fischer et al. US 6,267,990.

Fischer teaches a controlled release preparation comprising at least two populations of pellets: a first delayed release type of pellet; and a second delayed release type of pellet (abstract; claims). The ratio of the first and second delayed release type of pellet ranges from 1:2 to 1:7 (column 2, lines 10-14). The pellets of the first and second delayed release can be coated with the same materials, such as Eudragit or Aquacoat (column 2, lines 39-62).

Claims 63-65, 69-71, 76-82 and 85 are rejected under 35 U.S.C. 102(b) as being anticipated by Heinicke et al. US 5,834,024.

Heinicke teaches a controlled release formulation comprising short and long lag pellets of diltiazem (abstract). The diltiazem core is coated with polymer or mixture of polymers such as Eudragit S, Eudragit L, or Eudragit L 30D (column 5, lines 24-44). The thickness of the coating is increasing or decreasing to obtain the desired short and long lag pellets (column 4, lines 21-38). Example 1 shows the short lag pellet comprises about 12% weight gained of the coating polymer, and the long lag pellet comprises about 29% weight gained of the coating polymer. Heinicke further teaches the particle size of the pellet is about 1400 μm (example 1). The combined pellets are filled into capsule (column 6, line 64).

Claim Rejections - 35 USC § 103

Claims 63-65, 69-71, 76-82 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heinicke et al. US 5,834,024, in view of Fischer et al. US 6,267,990.

Heinicke is relied upon for the reason stated above. Heinicke further does not teach the claimed ratio of the short and long lag pellets. However, it would have been obvious to one of ordinary skill in the art to, by routine experimentation determine a suitable coating weight gain, as well as the ratio between the short and long lags depends in the release profile desired. This is because Heinicke teaches a controlled release dosage form effective to permit release of active agent at different cites in the GI tract over a 24 hours period, and because Heinicke teaches a weight gain of about

29%, with a mixture of 40% short lag and 60% long lag pellets (example 1). To be more specific, Heinicke is cited in view of Fischer for the teaching of the ratio of the short and long lag pellets.

Fischer teaches a controlled release preparation comprising at least two populations of pellets: a first delayed release type of pellet; and a second delayed release type of pellet (abstract; claims). The ratio between the first and second delayed release pellets ranges from 1:2 to 1:7 (column 2, lines 10-14). The pellets of the first and second delayed release can be coated with the same materials, such as Eudragit or Aquacoat (column 2, lines 39-62). Thus, it would have been obvious to one of ordinary skill in the art to optimize the controlled release composition of Heinicke to include the pellets population having the claimed ratio, because it is known in the art.

Claims 63-65, 69-71 and 76-91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Speirs US 5,834,021, in view of Andre et al. EP 1064938 A1.

Speirs teaches a controlled release dosage form comprising enterically coated pellet of prednisolone metasulphobenzoate incorporated into enterically coated capsule (abstract; and column 5, lines 61-67). Enteric coating polymer includes Eudragit S or Eudragit L (column 5, lines 9-34). The pellet has a diameter in the range of 700-1700 μm (column 4, lines 66-67). Spear further teaches that the thickness of the Eudragit coating on the pellets is between 15-30% based on the uncoated granule (column 5, lines 39-52).

Speirs does not expressly teach dosage form comprising plurality of particle with different release profiles.

Andre teaches a multiparticulate dosage form comprising active core, coating with film forming polymer such as Eudragit polymer (abstract; and paragraphs 0015-0017). Andre also teaches capsule comprising different population of coated multiparticulate dosage form with different release profiles (page 5, lines 38-43; and examples). Active agent includes prednisolone (paragraph 0024). Thus, it would have been obvious to one of ordinary skill in the art to modify the prednisolone dosage form of Speirs to prepare a dosage form with at least a timed pulse in view of the teachings of Andre. This is because Andre teaches that a timed pulse release dosage form allows targeting of a drug to a given site of the GI tract, in particular the colon (paragraph 0006), because Andre teaches a pulsed release dosage form that allows reduced dosing frequency, because Andre teaches a pulsed release dosage form suitable for drugs including prednisolone, and because Speirs teaches the desirability to include a plurality of the coated pellets in a capsule for the delivery of prednisolone to the intestine (column 4, lines 38-43).

Response to Arguments

Applicant's arguments filed 07/20/10 have been fully considered but they are not persuasive.

Applicant argues that Fischer et al. discloses using an undercoat (OPADRY II) between the surface of the pellets and the outer functional coating. Briefly, the purpose

of the undercoat is to seal the pellets to moisture and to smooth out the surface of the pellets so that the outer functional coating can be applied at uniform thickness as is conventional in the art of coating with pH-sensitive film forming polymers. However, in contrast to the present claims, Fischer et al. does not disclose an outer functional coating (i.e. a coating "comprising a pH dissolution dependent coating material") in direct contact with the surface of the pellets. (See pages 11-14 of the November l2, 2009, response for more detail).

However, in response to Applicant's arguments with respect to the OPADRY coating layer, the Examiner notes that Fischer cannot be limit to the teachings in Examples. The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain. In re Heck, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983). Fischer is relied upon for the teachings with in the four-wall patent. Neither the specification nor the claims in Fischer suggest applying an additional coating layer including the OPADRY layer. Further, as admitted by the Applicant, the OPADRY layer is merely the purpose of the undercoat is to seal the pellets to moisture. As known in the art, not all active agents are moisture sensitive, and therefore, not all active agents require the OPADRY layer. While Fischer teaches a wide variety of active agents, the Examples in Fischer only exemplify captopril as the active agent.

For at least the above reasons, the rejections over Fischer are maintained.

Applicant argues that Heinicke et al. does not teach or even suggest a coating comprising a pH dissolution dependent coating material in direct contact with the surface of the pellets. This has been acknowledged by the Examiner at the paragraph spanning pages 10 and 11 of the Office Action ("there is no disclosure in HEINICKE of coating the surface of a plurality of first and second pellets directly with a pH sensitive material as a film forming material for pH-mediated release of an active agent... "). (See pages 14-15 of the November 12, 2009, response for more detail).

In response to Applicant's argument that *the Examiner acknowledged that "there is no disclosure in HEINICKE of coating the surface of a plurality of first and second pellets directly with a pH sensitive material as a film forming material for pH-mediated release of an active agent... "* at the paragraph spanning pages 10 and 11 of the Office Action dated 01/15/10, however, to clarify the record, the statement that states that *"there is no disclosure in HEINICKE of coating the surface of a plurality of first and second pellets directly with a pH sensitive material as a film forming material for pH-mediated release of an active agent... "* is from the Applicant. See pages 14-15 of the Reply filed November 12, 2009. Further, Applicant's attention is called to the teachings at column 2, lines 32-44, where Heinicke teaches that active core is surrounded by a coating which has *only a single layer* (abstract). The Examples in Heinicke also show that the coating layer is immediately surrounding the core.

For at least these reasons, the rejections over Heinicke are maintained.

Applicant argues that neither Heinicke et al. nor Fischer et al. teach or suggest a coating comprising a pH dissolution dependent coating material in direct contact with the surface of the pellets. Similarly, neither Speirs nor Andre et al. teach or suggest a coating comprising a pH dissolution dependent coating material in direct contact with the surface of the pellets. For at least these reasons, the present claims are not obvious over the cited combinations of references.

In response to Applicant's arguments, however, the Examiner notes that Applicant did not specifically point out where in Speirs does the teaching that the core and the coating layer are not in direct contact. Contrary to the Applicant's arguments, Example V in Speirs teaches active cores are directly coated with a Eudragit coating.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:30 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. Tran/
Primary Examiner, Art Unit 1615